F TENT COOPERATION TRE Y

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/SG2004/000103	21.04.2004	21.04.2003

International Patent Classification (IPC) or both national classification and IPC
C12Q1/70

Applicant
GENOME INSTITUTE OF SINGAPORE

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/SG2004/000103

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☒ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The following document has not been furnished:

   ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. ☐ It has not been possible to consider the validity of the priority claim because a copy of the priority document was not available to the ISA at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

4. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-32 (all partially)

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 1-32 (all partially)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ not paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-32 (all partially) (invention 1)

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-32
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-32
Industrial applicability (IA)	Yes:	Claims	1-32
	No:	Claims	

2. Citations and explanations

   see separate sheet

Re Item IV

Lack of unity of invention

1 The present application relates to a plurality of inventions, or groups of inventions in the sense of Rule 13.1 PCT:

1.1 Invention 1: claims 1-32 (all partially)
Oligonucleotide consisting of SEQ ID NO: n, or comprising a nucleic acid having at least 90% sequence identity to SEQ ID NO: n or a complement thereof, and having a length of 100 or fewer nucleotides, method of detecting a severe acute respiratory syndrome (SARS) coronavirus in a sample comprising contacting nucleic acids from the sample with at least one primer comprising SEQ ID NO: n, method of determining a presence of a SARS coronavirus in a sample comprising contacting nucleic acids and/or amplicons thereof with at least one oligonucleotide that comprise SEQ ID NO: n or a variant having at least 90% sequence identity to SEQ ID NO: n or a complement thereof, composition, kit and system for detecting a SARS coronavirus comprising at least one oligonucleotide comprising SEQ ID NO: n or a variant having at least 90% sequence identity to SEQ ID NO: n or a complement thereof, and system comprising a computer or computer readable medium comprising a data set corresponding to SEQ ID NO: n or a variant having at least 90% sequence identity to SEQ ID NO: n or a complement thereof, wherein SEQ ID NO: n is SEQ ID NO: 1.

1.2 Inventions 2-21: claims 1-32 (all partially)
as for invention 1, wherein:
- for invention 2, SEQ ID NO: n is SEQ ID NO: 2;
- for invention 3, SEQ ID NO: n is SEQ ID NO: 3;
- for invention 4, SEQ ID NO: n is SEQ ID NO: 4;
- for invention 5, SEQ ID NO: n is SEQ ID NO: 5;
- for invention 6, SEQ ID NO: n is SEQ ID NO: 6;
- for invention 7, SEQ ID NO: n is SEQ ID NO: 7;
- for invention 8, SEQ ID NO: n is SEQ ID NO: 8;
- for invention 9, SEQ ID NO: n is SEQ ID NO: 9;
- for invention 10, SEQ ID NO: n is SEQ ID NO: 10;
- for invention 11, SEQ ID NO: n is SEQ ID NO: 11 or SEQ ID NO: 23;
- for invention 12, SEQ ID NO: n is SEQ ID NO: 12;
- for invention 13, SEQ ID NO: n is SEQ ID NO: 15;
- for invention 14, SEQ ID NO: n is SEQ ID NO: 16;

- for invention 15, SEQ ID NO: n is SEQ ID NO: 17;
- for invention 16, SEQ ID NO: n is SEQ ID NO: 18;
- for invention 17, SEQ ID NO: n is SEQ ID NO: 19;
- for invention 18, SEQ ID NO: n is SEQ ID NO: 20;
- for invention 19, SEQ ID NO: n is SEQ ID NO: 21;
- for invention 20, SEQ ID NO: n is SEQ ID NO: 22;
- for invention 21, SEQ ID NO: n is SEQ ID NO: 24.

2 The single general concept underlying the present application may be regarded as the provision of nucleic acids for the detection of a severe acute respiratory syndrome (SARS) coronavirus.

3 Drosten et al. (New England Journal of Medicine, 348 (20) 1967-1976, published on-line on 10-04-2003) and Ksiazek et al. (New England Journal of Medicine, 348 (20) 1953-1966, published on-line on 10-04-2003) disclose nucleic acids for the detection of a SARS coronavirus (Drosten et al.: Table 1, fig. 1B; the oligonucleotides SAR1S and SAR1As are also referred to in the present application as SEQ ID NO: 13 and SEQ ID NO: 14 (p. 69, l. 2 and l. 5); Ksiazek et al.: p. 1956, col. 1, SARS-specific primers Cor-p-F2, Cor-p-F3, Cor-p-R1).

4 In view of this prior art, the single general concept underlying the present application is not novel, and the problem solved by the present application may be regarded as the provision of further nucleic acids for the detection of a SARS coronavirus. The solutions proposed consist in each of the SEQ ID NO: 1-12 and 15-24.

5 In view of the above, and since the solutions brought to the problem appear to be technically unrelated and no other technical feature could be distinguished which, in light of the prior art, could be regarded as a special technical feature in the sense of Rule 13.2 PCT, the ISA is of the opinion that there is no single inventive concept unifying inventions 1-21 in the sense of Rule 13.1 PCT.

6 Consequently there is a lack of unity, contrary to the requirements of Rule 13.1 PCT. Since only invention 1 was subject of an International Search Report, the present written opinion is restricted to the subject-matter of said invention.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 Reference is made to the following documents:

D1: Drosten et al., New England Journal of Medicine 348 (20) 1967-1976, published on-line on 10-04-2003.

D2: Ksiazek et al., New England Journal of Medicine 348 (20) 1953-1966, published on-line on 10-04-2003.

D3: Database EMBL, Sequence Version Archive, SARS Coronavirus Tor2, complete genome, 15-04-2003, database accession number AY274119.1.

2 Novelty (Art. 33(2) PCT)

2.1 In view of the prior art cited, where no oligonucleotide of 100 nucleotides or less comprising a nucleic acid of sequence corresponding to SEQ ID NO: 1 or having at least 90% sequence identity with SEQ ID NO: 1 could be identified, the subject-matter of claims 1-32 is new.

3 Inventive step (Art. 33(3) PCT)

3.1 D1 and D2 constitute equally close prior art as to the independent claims 1, 2 or 7. The subject-matter of all three claims can be summarized as an oligonucleotide comprising a nucleic acid having at least 90% sequence identity to SEQ ID NO: 1 or a complement thereof, which oligonucleotide has 100 or fewer nucleotides.

3.1.1 D1 and D2 disclose oligonucleotides for the detection of a SARS coronavirus, which oligonucleotides have 100 or fewer nucleotides (D1: Table 1, fig. 1B; the oligonucleotides SAR1S and SAR1As are also referred to in the present application as SEQ ID NO: 13 and SEQ ID NO: 14 (p. 69, l. 2 and l. 5 of the present application); D2: p. 1956, col. 1, SARS-specific primers Cor-p-F2, Cor-p-F3, Cor-p-R1).

3.1.2 The subject-matter of claims 1, 2, or 7, differs in that the oligonucleotide comprises a nucleic acid having at least 90% sequence identity to SEQ ID NO: 1 or a complement

thereof, which oligonucleotide has 100 or fewer nucleotides.

3.1.3 The problem to be solved may therefore be regarded as the provision of alternative oligonucleotides comprising nucleic acids having at least 90% sequence identity to a sequence of the SARS coronavirus or a complement thereof, which oligonucleotide has 100 or fewer nucleotides.

3.1.4 The proposed solution is an oligonucleotide comprising a nucleic acid having at least 90% sequence identity to SEQ ID NO: 1 or a complement thereof, which oligonucleotide has 100 or fewer nucleotides.

3.1.5 This solution cannot be considered as involving an inventive step for the following reasons: several complete genome sequences of the SARS coronavirus were published before the priority date of the present application, see for instance D3. Providing alternative oligonucleotides for a known sequence falls within the art and abilities of the skilled person. An oligonucleotide as defined under item 3.1.2. is merely one of many alternatives that the skilled person would reach when trying to solve the problem posed. Accordingly, the subject-matter of claims 1, 2 and 7 does not involve an inventive step.

3.2 Dependent claims 3-6 and 8-12 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step.

3.3 Further, claims 13-32 do not contain any additional features which could confer an inventive step, the steps of the methods or components of the composition, kit and systems other than the oligonucleotides being well-known in the art. Accordingly, their subject-matter is also considered to lack inventive step for the same reasons.

4 Industrial applicability (Art. 33(4) PCT)

4.1 The subject-matter of claims 1-32 is considered to be industrially applicable.